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Original Article

Stroke in Children with Sickle Cell Disease: Prevalence, Pattern of Presentation and Outcomes in Jos, Nigeria

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ABSTRACT

Background: Stroke is a severe complication in children with sickle cell disease (SCD), leading to persistent disabilities and a markedly reduced quality of life. Most research on paediatric stroke in Nigerian children with SCD originates from low-altitude southern regions, leaving gaps regarding higher-altitude areas like Jos, Plateau State. This is important, as cerebral blood flow velocity has been shown to be influenced by altitude. We investigated the prevalence, presentation, and outcomes of stroke in children with SCD in Jos. **Methods:** A descriptive, retrospective study was conducted at Jos University Teaching Hospital from January 2018 to December 2022 using data from the paediatric haematology registry and hospital records. Records of children under 18 years were thoroughly reviewed for demographic details, stroke history, presentation, and outcomes. Stroke was diagnosed per WHO criteria, and analyses were performed using SPSS version 23.0. **Results:** Of 778 eligible children with SCD, 42 experienced stroke, yielding a prevalence of 5.4%. The mean age at first stroke was 7.7 ± 3.4 years, with 57.1% occurring in the 5–9-year group. Males comprised 57.1% of cases, and 57.1% belonged to the middle socioeconomic class. Clinically, all children exhibited limb weakness; hemiplegia was seen in 92.9% and aphasia in 42.9%. Concerningly, only 26.2% presented within 24 hours of symptom onset, and 40.5% had recurrent strokes. **Conclusion:** This study reveals a significant burden of paediatric stroke in Nigerian children with SCD. High recurrence rates, consistently delayed presentations, and limited imaging highlight the urgent need for early transcranial Doppler screening, improved preventive measures, and better healthcare access to reduce the stroke burden.

Keywords: Pediatric Stroke, Sickle Cell Disease, Transcranial Doppler Screening, Stroke Recurrence, High-Altitude Health Outcomes

INTRODUCTION

Sickle cell disease (SCD) is a genetic disorder with significant global public health implications, particularly affecting sub-Saharan Africa, including Nigeria, where prevalence, morbidity, and mortality rates remain high. [1-3] Stroke, or cerebrovascular accident (CVA), is among the most severe complications in children with SCD.[4] Stroke is defined as acute neurological dysfunction due to cerebral artery occlusion or haemorrhage, resulting in neurological symptoms lasting over 24 hours. [4]

Stroke frequently causes persistent disabilities such as motor impairment, cognitive dysfunction, language deficits, and reduced quality of life. [5-8] Children affected by stroke may also experience sensory deficits

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and emotional distress, and may impose substantial financial burdens on their families.[7, 8] However, stroke in SCD is largely preventable through early identification using transcranial Doppler (TCD) ultrasonography, a sensitive, non-invasive screening method.[9] Unfortunately, access to TCD screening remains limited in most health facilities in low-middle-income countries including facilities in Plateau State, North Central Nigeria. [10]

Current research on paediatric stroke in Nigerian children with SCD predominantly comes from southern, low-altitude regions, leaving significant gaps in understanding stroke prevalence, presentation, and outcomes in higher-altitude areas like Jos, Plateau State. This is particularly relevant, as cerebral blood flow velocity has been shown to vary with altitude. [11-15] Addressing these gaps is essential for developing effective preventive strategies and targeted interventions. This study aims to investigate the prevalence, pattern of presentation, and outcomes of stroke in children with SCD attending Jos University Teaching Hospital. The findings are expected to support advocacy for improved preventive care, diagnostic access, and better paediatric stroke management.

METHODS

Study Design and Setting

This was a descriptive, retrospective study designed to determine the prevalence, pattern of presentation, and outcomes of stroke among children with sickle cell disease seen at the Paediatric Haematology/Oncology Unit of Jos University Teaching Hospital (JUTH), covering five years from January 2018 to December 2022.

Jos University Teaching Hospital is a large referral hospital in Jos, the capital city of Plateau State. It receives referrals from all parts of the state. Plateau State encompasses a broad range of elevations; Jos, the capital city, is situated at an elevation of approximately 1,295 meters (4,250 feet) above sea level, contributing to its relatively cooler climate compared to other regions in Nigeria. Plateau State is located in Nigeria's North Central region, covering approximately 26,000 km². [16]

The Paediatric Haematology/Oncology unit provides both inpatient and outpatient care for children with SCD. The unit runs a weekly sickle cell clinic attended by about 50-60 patients per session and keeps a registry that archives all sickle cell-related events in patients both at admission and during clinic visits.

Study Population

All children (younger than 18 years) with sickle cell disease (confirmed by cellulose acetate haemoglobin electrophoresis) whose data were captured on the unit registry between January 2018 to December 2022 were included in the study. Those with missing or incomplete information were excluded while patients diagnosed with transient ischemic attacks, seizures without neurological deficits, meningitis, or encephalitis were also excluded.

Sample Size Determination

The sample size was calculated using the formula for cross-sectional studies ($n = Z^2pq/d^2$) [17], where n = minimum required sample size, Z = 1.96 (standard normal deviate at 95% confidence level), p = 2.9% (prevalence of stroke from a previous study)[14], $q = 1 - p = 0.971$, and d = 0.05 (precision of the study). Substituting these values, the calculated minimum sample size was 44. However, as this study utilized registry data and patients' hospital records, all available records that met the inclusion criteria were included, yielding a final sample size of 42 patients after excluding 3 records due to incomplete data.

Data Collection

Following identification of patients with a diagnosis of stroke (CVA) from the registry, their clinical records were retrieved to obtain additional clinical information. Two trained research assistants extracted data from individual patient records using a pre-tested proforma developed for the study. The lead investigator reviewed and validated all entries to ensure accuracy and completeness.

Extracted data included demographic information, haemoglobin genotype, age at first stroke occurrence, timing of hospital presentation, number of stroke episodes, side of brain involvement, clinical manifestations, results of brain imaging (where available), treatment received, and clinical outcomes.

Operational Definitions / Grading of Responses

Stroke diagnosis was based on clinical criteria defined by the World Health Organization (WHO): "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 h or longer or leading to death with no apparent cause other than of vascular origin'' [18]

The side of brain involvement was inferred based on the laterality of limb weakness—right-sided limb

weakness indicated involvement of the left cerebral hemisphere, and vice versa. [19]

In this study, presentation to the hospital was classified as 'late or delayed' if it occurred more than 24 hours after the onset of stroke symptoms, and as 'early' if within 24 hours. The stroke clinical outcome was determined based on documentation in the patient's medical records at least one year following the initial stroke event.

The socioeconomic status of the patients was assessed using the Olusanya et al. index scoring method, which classifies individuals based on parental education and occupation. [20]

Data Analysis

Statistical analysis was performed using SPSS version 23.0 (IBM, Chicago, IL). Descriptive statistics (frequencies and percentages) were used to summarize categorical variables like sex, haemoglobin genotype, and stroke classification. Continuous variables, such as age at stroke diagnosis, were summarized using means and standard deviations. The WHO clinical definition of stroke was applied consistently across cases.

Ethical Considerations

Ethical approval was obtained from the Health Research Ethics Committee of Jos University Teaching Hospital.

RESULTS

Characteristics of Children with Sickle Cell Disease and Stroke

Of the 45 patients with sickle cell disease and stroke, 42 children were included in the study, while 3 were excluded due to incomplete data. The mean age at first stroke was 7.7 ± 3.4 years, with the youngest case occurring at 1.75 years and the oldest at 17 years. The majority of strokes (57.1%) occurred in the 5–9-year age group, while only 7.1% were observed in children older than 15 years. Males accounted for 57.1% of the cases, and more than half of the children (57.1%) belonged to the middle socioeconomic class. Additionally, 95.2% of the children (n = 40) resided in Jos, while 4.8% (n = 2) lived outside the city. Most children (97.6%) had the HbSS genotype, while 2.4% had HbSS with persistent fetal hemoglobin (HbSS+F). No cases of HbSC were recorded (Table 1).

Table 1: Characteristics of Children with Sickle Cell Disease and Stroke

Characteristics	Frequency (n = 42)	Percentage
Age at 1st stroke (years)		
<5	8	19.0
5-9	24	57.1
10-14	7	16.7
>15	3	7.1
Mean age at 1st stroke 7.7 ± 3.4 years	Min 1.75, Max 17 years	
Sex		
Male	24	57.1
Female	18	42.9
Socioeconomic status		
Low	12	28.6
Middle	24	57.1
High	6	14.3
Residential Address		
Within Jos metropolis	40	95.2
Outside Jos metropolis	2	4.8
Haemoglobin phenotype		
Hb SS	41	97.6
Hb SS + F	1	2.4
Hb SC	0	0.0

Hb - Haemoglobin

Prevalence of Stroke

Of the 801 patient records captured in the registry between January 2018 and December 2022, twenty were excluded because the patients were 18 years or older (not yet transitioned to adult care). Additionally, three patients with a diagnosis of stroke were excluded due to incomplete hospital records. The overall prevalence of stroke among children with sickle cell disease in this study was 5.4% (42/778) (Figure 1).

Pattern of Stroke Presentation

Of the 42 children studied, 25 (59.5%) experienced a single stroke episode, while 17 (40.5%) had recurrent strokes. Only 11 children (26.2%) presented within 24 hours of stroke onset, while 31 (73.8%) had a delayed presentation. Some of the reasons documented in the case notes for the delayed hospital presentation included caregivers' failure to recognize the illness's severity, initial management at lower-tier health facilities for non-stroke conditions and seeking spiritual interventions before medical care. The left hemisphere was affected in 50% of cases, the right hemisphere in 42.9%, and bilateral involvement was noted in 7.1%. Importantly, none of the children were on hydroxyurea therapy prior to their first stroke.

The most common clinical manifestation was limb weakness, which was present in all the 42 cases (100%). Hemiplegia was the predominant form (39, 92.9%), while a few children had quadriplegia in 3 cases (7.1%). Other commonly reported symptoms included aphasia (18 children, 42.9%), slurred speech (14, 33.3%), and facial nerve palsy (13, 31.0%). Less frequent

manifestations included headache (10, 23.8%), convulsions (7, 16.7%), unconsciousness (7, 16.7%), dizziness (4, 9.5%), and visual loss (2, 4.8%).

Radiological evaluation using CT scan was performed in only 3 children (7.1%), while the remaining 39 (92.9%) did not undergo brain imaging test. See Table 2.

Table 2: Pattern of Presentation of Stroke Among the Study Population (n = 42)

Characteristics	Frequency (%)
Number of stroke occurrence	
1	25 (59.5)
2	14 (33.3)
3	1 (2.4)
4	2 (4.8)
Timing of presentation after onset of stroke	
Within 24 hours	11 (26.2)
>24hours to 72 hours	14 (33.3)
>72 hours	17 (40.5)
Side of the brain affected	
Left hemisphere	21(50.0)
Right hemisphere	18 (42.9)
Both [x]	3 (7.1)
Already on hydroxyurea before occurrence of first stroke	
Yes	0 (0.0)
No	42 (100)
Clinical presentation	
Limb weakness	42 (100.0)
Hemiplegia	39 (92.9)
Quadriplegia	3 (7.1)
Aphasia	18 (42.9)
Slurred speech	14 (33.3)
Facial nerve palsy	13 (31.0)
Headache	10 (23.8)
Convulsion	7 (16.7)
Unconsciousness/coma	7 (16.7)
Dizziness	4 (9.5)
Visual loss	2 (4.8)
Irrational behaviour	1(2.4)
Radiological investigation (CT scan) done	
Yes	3 (7.1%)
No	39 (92.9%)

X – Recurrent stroke, first stroke was on the left hemisphere in two of the subjects and on the right in the third subject
CT – Computed Tomography

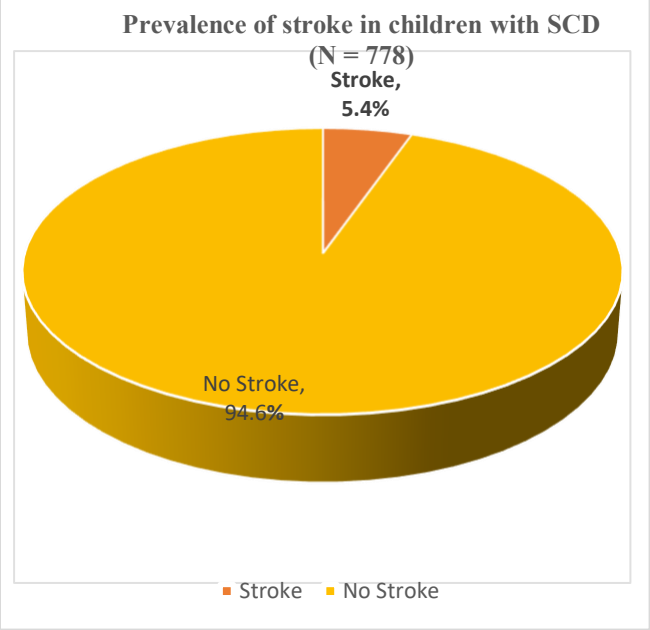

Figure 1: Prevalence Of Stroke in Children with Sickle Cell Disease

Table 3: Treatment, Recurrence Patterns and Outcomes of Stroke in the Study Population

Characteristics	Frequency (%) n= 42
Treatment received	
Exchange blood transfusion at presentation	21(50.0)
Chronic transfusion	20 (47.6)
Physiotherapy	26(61.9)
Hydroxyurea	24 (57.1)
Outcome of stroke	
Residual limb weakness	26 (61.9)
Residual facial nerve palsy	4 (9.5)
Residual slurred speech	5 (11.9)
Decline in academic performance (n=34)	12(35.3)
Lost to follow up	9 (21.4)
Seizure disorder	2(4.8)
Death[y]	3 (7.1)
Recurrent strokes before first hospital presentation	
Yes	14 (33.3)
No	28 (66.7)
Recurrence after chronic blood transfusion and/ or hydroxyurea (n=24)	
Yes	3 (12.5)
No	21(87.5)

y – Not during the acute stroke event

Treatment, Recurrence Patterns and Outcomes of Stroke in The Study Population

Out of the 42 children with stroke, 21 (50.0%) received exchange blood transfusion at the time of stroke presentation, while 20 (47.6%) were subsequently placed on chronic transfusion therapy. Physiotherapy was administered to 26 children (61.9%), and 24 (57.1%) were commenced on hydroxyurea therapy as part of their long-term management.

At the clinic follow-up conducted at least one year after the stroke, 26 children (61.9%) had persistent limb weakness, while 5 (11.9%) continued to have slurred speech. A decline in academic performance was reported in 12 of 34 children (35.3%) for whom data were available. Other residual deficits included facial nerve palsy in 4 children (9.5%) and seizure disorders in 2 (4.8%).

Recurrent strokes prior to initial hospital presentation were documented in 14 children (33.3%). Despite initiation of chronic transfusion and/or hydroxyurea in 24 children, 3 (12.5%) experienced another stroke while on treatment. Regarding overall outcomes, 9 children (21.4%) were lost to follow-up, and 3 (7.1%) died during the study period (Table 3).

DISCUSSION

Our study set out to determine the prevalence, pattern of presentation, and outcomes of stroke among children with sickle cell disease in Jos, Plateau State, North Central Nigeria—an area of relatively high altitude with historically limited data.

This study found a stroke prevalence of 5.4% among children with sickle cell disease attending Jos University Teaching Hospital in Nigeria. This figure is comparable to those reported in other parts of the country and internationally. For instance, Fatunde et al [13] in Ibadan (Southwestern Nigeria) also reported a prevalence of 5.4%, while a study in Abuja documented a similar rate of 5.2%. [5] Slightly lower rates were observed in Port Harcourt, where a prevalence of 4.3% was documented, [12] and in the United States, where Ohene-Frempong et al reported 4.01%. [4] On the other hand, higher figures were seen in Jamaica (7.8%), [21] Uganda (6.8%), [22] and another study from Ibadan (6.8%). [11] Interestingly, a multicenter Nigerian study involving 11 centers reported a much lower prevalence of 7.4 per 1,000 children, reflecting significant variability across different settings. [23]

Interestingly, despite Jos, Plateau State's higher altitude (approximately 1,295 meters above sea level), [16] which theoretically could increase stroke risk due to relative hypoxia and increased blood viscosity, [15, 24] our prevalence rate remains consistent with those from lower-altitude regions. [5, 13,,] This finding suggests that prolonged residence in high-altitude conditions might lead to physiological adaptations, potentially mitigating expected increases in stroke incidence. [25] It is conceivable that chronic exposure to mildly hypoxic conditions may stimulate compensatory mechanisms, such as increased hemoglobin F levels, changes in vascular physiology, or improved oxygen affinity, which might reduce stroke risk. [25]

However, this study did not directly measure such physiological adaptations, and further research is required to confirm whether long-term acclimatization indeed influences stroke risk in paediatric SCD populations residing at higher altitudes.

Additionally, the variability in prevalence rates observed in different studies could reflect differences in methodological approaches, including study design, sample size, diagnostic criteria, healthcare infrastructure, availability and use of preventive interventions like transcranial Doppler (TCD) screening, and socio-economic factors influencing healthcare access and utilization.

The mean age at first stroke in our study was 7.7 ± 3.4 years, with ages ranging from 1.75 to 17 years. The most commonly affected age group was 5–9 years, accounting for 57.1% of cases. This pattern is consistent with previous reports from Port Harcourt in South-Southern Nigeria (5–10 years), [12] Uganda (2–10 years, with a mean of 6.1 years), [22] and two studies from Ibadan in South-Western Nigeria—one reporting a mean age of 6.8 years and the other, 81.4 ± 37.2 months.[11,13] Stroke occurrence at such young ages has significant implications. These include lifelong neurological deficits, compromised academic achievement, and substantial social and economic burdens on families and society.

Gender analysis in this study showed a higher incidence of stroke among males. This finding is consistent with reports from Port Harcourt and Jamaica. [12, 21] In contrast, the Ugandan study found an equal distribution between males and females. The reasons why stroke appears to be more common in males are not entirely clear, but possible explanations include genetic or hormonal factors. This observation definitely calls for further research.

The recurrent stroke rate in our study was notably high at 40.5%. This exceeds rates reported in studies from Port Harcourt (18.2%), Ibadan (26.1%), and a multicenter Nigerian study (23%), though it remains lower than those documented in Uganda (46%) and by Fatunde et al. in Ibadan (61.5%). [11-13, 22-23] These findings reflect gaps in secondary prevention, limited follow-up, and poor adherence to disease-modifying therapies such as hydroxyurea and chronic transfusion, all of which are essential to reducing stroke recurrence.

In our study, we found left hemispheric strokes to be more prevalent than right-sided ones.This is consistent with findings in the literature.[26, 27] . Several factors

contribute to this observation: the left hemisphere's elevated metabolic demands render it more susceptible to ischemic injury during reduced cerebral blood flow; [28] large-vessel ischemic strokes occur more frequently in the left middle cerebral artery territory; [26] and speech impairments resulting from left-sided strokes are more noticeable, leading to quicker recognition and diagnosis . [27] Additionally, left-sided strokes are often associated with more severe deficits, higher NIH Stroke Scale (NIHSS) scores at admission, and increased mortality, underscoring the importance of timely recognition and prompt, aggressive management. [26]

Clinical presentations in our study predominantly included limb weakness (100%), hemiplegia (92.9%), aphasia (42.9%), slurred speech (33.3%), and facial nerve palsy (31.0%). These findings are consistent with previous studies. For instance, limb weakness was reported in 97.1% of cases by Obama et al, while George et al. reported a lower incidence of 45.5%. [12, 29] George et al. also reported higher occurrences of convulsions (54.5%) compared to our 16.7%, and coma/unconsciousness was similarly reported at 18.2% by George et al. compared to our 16.7%. [12] Our results highlight the clinical diversity and severity of paediatric stroke manifestations, emphasizing the necessity of prompt recognition and intervention.

Regarding the timing of hospital presentation, 73.8% of children presented late, primarily due to caregivers' (and in some instances, healthcare providers') inability to recognize stroke symptoms, misunderstanding of the emergency nature of stroke, and misattribution of stroke symptoms to spiritual attacks necessitating spiritual rather than medical intervention. These delays significantly impact patient outcomes, leading to missed opportunities for acute interventions like exchange blood transfusions, increasing the risk of permanent neurological deficits, and adversely affecting overall prognosis.

Treatment guidelines recommend immediate exchange blood transfusion (EBT) within 2 hours of presentation for patients with Hb levels above 8.5g/dl, or a top-up transfusion prior to EBT if Hb levels are below 8.5g/dl. [30] EBT should ideally be performed within 72 hours of stroke onset. In our study, however, only 50% of patients underwent immediate EBT, primarily due to delayed presentation (sometimes 2-4 weeks post-stroke), financial constraints in procuring blood, and occasional refusal of blood transfusion by caregivers. Chronic transfusion therapy was similarly affected by significant financial barriers, leading to inconsistent adherence to this intervention. These limitations significantly increase the risk of recurrent stroke, prolonged neurological impairment, and poor clinical outcomes. To address these barriers, public education campaigns to improve early stroke recognition, government subsidies for transfusion services, and comprehensive healthcare insurance coverage are essential.

Due to financial constraints and limited availability, only three patients in our study had brain imaging. This led to a reliance primarily on clinical diagnosis. Consequently, this limitation restricted our ability to distinguish between ischemic and hemorrhagic strokes. The inability to accurately determine stroke type can impede optimal management and may influence outcomes negatively. Improved healthcare funding, subsidized imaging costs, and enhanced availability of diagnostic services could address these barriers and thereby allowing more precise diagnoses and tailored treatments.

Outcomes in our study revealed substantial residual deficits, with residual limb weakness (61.9%), facial nerve palsy (9.5%), and slurred speech (11.9%). Notably, 35.3% experienced a decline in academic performance, highlighting significant cognitive impacts. Similar outcomes, such as mortality rates, were comparable with those reported by Fatunde et al (7.2%) and George et al (9.1%). [12, 13] Importantly, we observed that recurrent strokes appeared to be associated with increased cognitive decline and motor deficits among our study population. [31]

The high stroke prevalence and recurrence rates observed in this study bring to light the importance of effective primary and secondary stroke prevention strategies. Primary prevention through routine transcranial Doppler screening, proactive hydroxyurea therapy, and caregiver education about early signs of stroke are required. [9, 10] Equally, robust secondary prevention measures, including consistent chronic transfusion programs, regular hydroxyurea use, and structured medical follow-ups, are essential in minimizing recurrent strokes and associated neurological deficits. [10]

Limitations

This study has some limitations, including its retrospective design, limited use of brain imaging due to financial and availability constraints, and being conducted in a single center. These factors restrict precise stroke classification, diagnosis, and generalizability of findings. Multi-center prospective studies could provide further insights.

CONCLUSION

This study highlights a significant prevalence and a high recurrence rate of stroke among children with SCD in Jos, Nigeria. Our findings highlight the urgent need for enhanced stroke management strategies. Primary and secondary prevention measures, improved healthcare infrastructure, and targeted policies could significantly

mitigate stroke-related morbidity and mortality in this population.

Acknowledgements

The authors would like to thank Queen Bello-Ayodeji and Cecilia Akolo for the data collection.

African Research and Innovative Initiative for Sickle Cell Education (ARISE)

All the activities related to this research have been performed in compliance with the applicable national/local rules and respecting participants' rights. The training on statistical methodology, data analysis and manuscript writing has been received in the framework of the ARISE project.

Disclosures

The lead researcher received sickle cell disease management and research training through the European Union–funded ARISE project (H2020-MSCA-RISE-2018) in the United Kingdom. The study was funded by the researchers.

Conflict of Interest

There is no conflict of interest.

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